## REMARKS

The Examiner rejected claims 1-7, 9, 11-22, 24, 26, 28-30, and 33. Claim 22 has been amended herein to depend from claim 20 as opposed to claim 21. In addition, claim 33 has been cancelled herein without prejudice. No new matter has been added.

In light of the following remarks, Applicants respectfully request reconsideration and allowance of claims 1-7, 9, 11-22, 24, 26, and 28-30.

Examiner Interview

Applicants thank Examiner Lucas and Examiner Housel for the courtesy of the interview on April 26, 2006. The substance of this interview involved the rejections and comments presented herein. During the interview, the Examiners requested submission of evidence such as published manuscripts to demonstrate the selective ability of using attenuated measles viruses to reduce the number of viable cancer cells in a mammal. The Examiners also requested submission of evidence to demonstrate the ability of different strains of attenuated measles viruses to reduce the number of viable cancer cells in a mammal. Four published manuscripts and one manuscript recently accepted for publication are attached hereto and listed on the accompanying Information Disclosure Statement. Applicants respectfully request consideration of this material since Applicants are providing information requested by the Examiners. *See*, 37 C.F.R. § 105.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-7, 9, 11-22, 24, 26, 28, 29, and 33 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement and written description. Both rejections appear based on an alleged inability of attenuated measles viruses, other than the attenuated measles viruses used in the Example section of Applicants' specification, to reduce the number of viable cancer cells in a mammal.

Applicants respectfully disagree. For all the reasons of record, a person having ordinary skill in the art reading Applicants' specification at the time of filing would have been able to make and use the presently claimed invention without undue experimentation and would have appreciated that Applicants invented the presently claimed subject matter and were in possession

of the invention as claimed. As additional evidence of Applicants' compliance with the requirements of 35 U.S.C. § 112, first paragraph, Applicants respectfully submit two published manuscripts, which confirm the ability of other attenuated measles viruses to reduce the number of viable cancer cells within a mammal. The first publication, Myers *et al.* (*Cancer Gene Therapy*, 12:593-599 (2005)), has eleven authors, two of whom are listed inventors on the present patent application. This reference demonstrates that the Moraten strain of attenuated measles viruses effectively reduces the number of viable ovarian cancer cells within a mammal to a level comparable to that observed with an Edmonston B strain of attenuated measles viruses even though the Moraten strain of attenuated measles viruses exhibited reduced *in vitro* fusion kinetics compared to the Edmonston B strain of attenuated measles viruses. In fact, the second paragraph on page 596 states that "[i]nterestingly, while MV-Moraten was the slowest at inducing cpe [cytopathic effects] *in vitro* (Fig 2a), its antitumor efficacy was comparable to that of MV-CEA."

The second publication, Heinzerling *et al.* (*Gene Therapy*, 106:2287-2294 (2005)), has six authors, none of whom is listed as an inventor on the present patent application. This publication demonstrates that an Edmonston-Zagreb vaccine strain of attenuated measles viruses effectively reduces the number of viable T-cell lymphoma cancer cells within a mammal. For example, the results section starting on page 2290 discloses that intralesional injection of an Edmonston-Zagreb vaccine strain of attenuated measles viruses after IFN-$\alpha$ treatment is well tolerated and leads to regression of tumor lesions in humans. Taken together, these publications demonstrate the ability of different strains of attenuated measles viruses to reduce the number of viable cancer cells in a mammal. Thus, Applicants' specification fully enables and adequately describes the presently claimed invention.

In light of the above, Applicants respectfully request withdrawal of the rejections of claims 1-7, 9, 11-22, 24, 26, 28, and 29 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-7, 9, 11-22, 24, 26, and 28-33 under 37 U.S.C. § 103(a) as allegedly being obvious in light of the various combinations of references as indicated in the record.

Applicants respectfully disagree with these rejections. For all the reasons of record, a person having ordinary skill in the art reading the cited references would not have been motivated to carry out the presently claimed methods. As additional evidence of the non-obviousness of the presently claimed invention, Applicants respectfully submit two published manuscripts and a manuscript recently accepted for publication. These manuscripts demonstrate the selective nature of using attenuated measles viruses to reduce the number of viable cancer cells in a mammal. The first manuscript, Ong *et al.* (accepted for publication in *Experimental Hematology*), has six authors, two of whom are listed inventors on the present patent application. This manuscript provides data indicating that attenuated measles viruses are selective for cancer cells and not normal cells even though all nucleated human cells are reported to express CD46, a receptor for attenuated measles viruses. For example, the result section starting on page 10 discloses testing tumor selectivity against human primary myeloma cells isolated by CD138 cell sorting. In particular, the authors state that:

> Rapid replicative spread of the virus in the CD138+ culture gave rise to the characteristic measles virus-induced cytopathic effect of cell-to-cell fusion with formation of large multinucleated syncytia (Fig. 3A). . . . Syncytium formation was minimal in CD138- cultures (Fig. 3), and no cytopathic effect was seen with prolonged culture to 5 days after infection (Fig. 3A). Thus, MV infection was restricted in NPCs [non plasma cells] but was efficient in myeloma cells which were selectively killed by the virus.

The second manuscript, Peng *et al.* (*Blood*, 98:2002-2007 (2001)), published with six authors, two of whom are listed inventors on the present patent application. This publication also provides data indicating that attenuated measles viruses are selective for cancer cells and not normal cells. For example, the first paragraph of the results section on page 2003 states that "MV-eGFP grew efficiently and selectively in all the myeloma cells tested, whereas virus growth was severely restricted in primary cultures of PHA-stimulated PBLs (Table 1), normal dermal fibroblasts, and vascular smooth muscle cells (data not shown)."

The third manuscript, Peng *et al.* (*Cancer Research*, 62:4656-4662 (2002)), was published with six authors, two of whom are listed inventors on the present patent application. Like the Ong *et al.* manuscript and the Peng *et al. Blood* publication, this publication provides data indicating that attenuated measles viruses are selective for cancer cells and not normal cells.

For example, under the section entitled "MV-hCEA Was Selectively Oncolytic for Ovarian Cancer Cells and Had Minimal Cytopathic Effects on Normal Cells" on page 4659, the authors state that:

> Large multinucleated (>40 nuclei) syncytia were seen in SKOV3ip.1, OV202, and OV207 ovarian tumor cultures by 48 h after infection. These syncytia eventually became nonviable and floated off from the tissue culture plates. In contrast, no such syncytia nor cytotoxic effects were seen in the normal dermal fibroblasts, nontransformed OSE cells, or mesothelial cells (Fig. 3).

Taken together, these manuscripts demonstrate the selective ability of using attenuated measles viruses to reduce the number of viable cancer cells in a mammal, thereby providing additional evidence in support of the non-obviousness of the presently claimed invention.

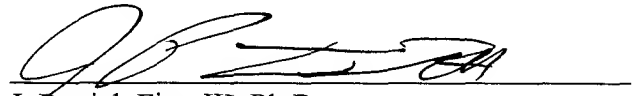
In light of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

## CONCLUSION

Applicants submit that claims 1-7, 9, 11-22, 24, 26, and 28-30 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned attorney at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

Date: May 5, 2006



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